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09/308,080	10/28/99	GONZALEZ F	15280-271100

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1652	10

DATE MAILED: 04/18/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary	Application No.	Applicant(s)	
	09/308,080	GONZALEZ ET AL.	
	Examiner	Art Unit	
	David J. Steadman	1652	

-- The MAILING DATE of this communication appears on th cov r she t with the corr spondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-19 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-19 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

Status of the Application

Claims 1-19 are pending.

Applicants' election with traverse of Group I, claims 1-5 and 10-14 in Paper No. 9, filed 03/06/01 is acknowledged. It is noted that the Examiner listed the claims of Group I as 1-5 and 10-14 in the restriction/election mailed 12/27/00. However, the claims of Group I should have been listed as 1-5 and 10-19. Therefore, Applicants' election with traverse of Group I, claims 1-5 and 10-19 is acknowledged. Upon reconsideration of the restriction requirement in view of the similar subject matter presented in the claims of Groups I and II, the restriction of claims into Group I (claims 1-5 and 10-19) and Group II (claims 6-9) is removed.

Drawings

1. The drawings submitted with this application have not been reviewed by a draftsperson at this time. When formal drawings are submitted, the draftsperson will perform a review. Direct any inquiries concerning drawing review to the Drawing Review Branch (703) 305-8404.

Sequence Compliance

2. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825; applicants' attention is directed to the final rulemaking notice

published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). To be in compliance, applicants must provide an initial computer readable form (CRF) copy of the "Sequence Listing", an initial paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification, and a statement that the content of the paper and CRF copies are the same and, where applicable, include no new matter as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.821(b) or 1.825(d). Applicant is requested to return a copy of the attached Notice to Comply with the response.

Specification/Informalities

3. The disclosure is objected to because of the following informalities: 1) Figures 1A and 1B are present in the application, therefore, the "Brief Description of the Drawings" section should recognize both Figures 1A and 1B; 2) oligonucleotide primers listed at pages 21 and 24 include sequence listings that should be identified by a specific SEQ ID NO. Appropriate correction is required. See "Sequence Compliance" section above.

4. It is noted by the Examiner that Applicants claim priority from provisional application number 60/013,835 in the Declaration. However, an amendment to the first paragraph of the specification has not been provided. In order for Applicants to claim priority from provisional application number 60/013,835, Applicants should provide an amendment to the first paragraph of the specification stating claimed domestic priority.

5. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Claim Objections

6. Claims 8 and 10 are objected to because of the following informalities: the terms "a primer which hybridize to" and "genomic DNA for dihydropyrimidine" are grammatically incorrect and should be replaced with, for example, "a primer which hybridizes to" and "genomic DNA for a dihydropyrimidine", respectively. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-9, 13, 14, and 17-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

8. Claims 1 (claims 2-5 dependent thereon) and 6 are indefinite in the recitation of "intron-exon boundary". It is noted that Applicants have provided a definition of "intron-exon boundary" however, it is unclear from this "definition" as to the scope of the term "intron-exon boundary". It is suggested that Applicants clarify the meaning of the term "intron-exon boundary" by specifying nucleic acid residues of the human genomic DPD DNA that Applicants consider the "intron-exon boundary".

9. Claims 2 and 7 are indefinite in the recitation of "the region flanking the exon which encodes amino acids 581-635" as it is unclear as to the exact location of "the region flanking the exon which encodes amino acids 581-635". It is suggested that Applicants clarify the meaning of "the region flanking the exon which encodes amino

acids 581-635" by specifying nucleic acid residues of the human genomic DPD DNA that Applicants consider the flanking region.

10. Claims 3, 4, 8, 9, 13, 14, and 17-19 are rejected as being not sequence compliant because these claims refer to nucleic acid sequences but do not recite the corresponding SEQ ID NOs of primers DELF1 and/or DELR1.

11. Claims 3, 8, 13, 14, 18, and 19 are indefinite in the recitation of "stringent conditions" as the specification does not define what conditions constitute "stringent". It is noted that a definition of "stringency" is provided in the specification at pages 6-7, however, it is unclear from this "definition" as to the scope of the term "stringent conditions". What hybridization conditions are considered "stringent" varies widely in the art depending on the individual situation as well as the person making the determination. As such it is unclear how homologous to the sequence of primer DELF1 (claim 18) or DELR1 (claim 19), the sequence of a PCR primer must be to be included within the scope of these claims.

12. Claims 18 and 19 recite the limitation "the composition" in claim 15. There is insufficient antecedent basis for this limitation in the claim. It is suggested that the term "the composition" be replaced with, for example, "the kit".

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 1-19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1 (claim 5 dependent thereon), 2 (claim 4 dependent thereon), 3, 6, 7 (claim 9 dependent thereon), 8, 10 (claims 13 and 14 dependent thereon), 11, 12, 15 (claims 17-19 dependent thereon), and 16 are directed to methods of detecting splicing defects and methods of screening patients for sensitivity to 5-fluorouracil by analyzing an intron-exon boundary for an exon that encodes amino acids 581-635 of a corresponding wild-type DPD or compositions and kits comprising PCR primers that bind to a DPD gene. The specification teaches only a single representative species of a DPD gene, i.e., a human DPD gene, a single representative species of splicing defects in a genomic DNA encoding amino acids 581-635 of DPD, i.e., a G to A transition at nucleotide 1987 of genomic DPD DNA, or a single representative species of PCR primers that bind to DNA either 3' or 5' of a splice site in the genomic DNA for a DPD gene for an exon encoding amino acids 581-635, i.e., DELF1 and DELR1, respectively. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the description of being a DPD gene, a splicing defect, or the functionality of PCR primers that binds to DNA either 3' or 5' of a splice site in the genomic DNA for a DPD gene for an exon encoding amino acids 581-635. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

14. Claims 1-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for 1) a method of detecting a splicing defect in a human DPD gene, comprising determining whether a G to A transition occurs at nucleotide 1987 of genomic DNA encoding human DPD; 2) a method of screening patients for sensitivity to 5-fluorouracil, comprising determining whether a G to A transition occurs at nucleotide 1987 of the patient's genomic DNA encoding human DPD; 3) a composition comprising a first PCR primer with the sequence 5'-TGCAAATATGTGAGGAGGGACC-3' and a second PCR primer with the sequence 5'-CAAAGCAACTGGCAGATTC-3'; and 4) a kit comprising a container, a first PCR primer with the sequence 5'-TGCAAATATGTGAGGAGGGACC-3', and a second PCR primer with the sequence 5'-CAAAGCAACTGGCAGATTC-3', does not reasonably provide enablement for: a method of detecting a splicing defect in a DPD gene, comprising determining whether any genomic DNA encoding a DPD gene has a wild-type intron-exon boundary for an exon which encodes amino acids 581-635 for a corresponding wild-type DPD or a method of screening patients for sensitivity to 5-fluorouracil, comprising isolating a genomic DNA from the patient which encodes the DPD gene and determining whether the gene has a wild-type intron-exon boundary for an exon which encodes amino acids 581-635 for a corresponding wild-type DPD, and optionally, wherein the method comprises the step of amplifying intronic genomic DNA encoding the DPD in the region flanking the exon that encodes amino acids 581-635, and optionally, wherein the method comprises amplifying the genomic DNA with a primer that hybridizes to a DPD intronic nucleic acid that hybridizes to a primer selected from the group of primers consisting of DELF1 and DELR1 under stringent conditions; a

composition comprising first and second PCR primers that bind to DNA 3' or 5', respectively, of a splice site in the genomic DNA for a DPD gene for an exon encoding amino acids 581-635, and optionally wherein the first and second PCR primers bind to intronic DPD DNA, and optionally wherein the first and second PCR primers hybridize under stringent conditions to nucleic acids complementary to DELF1 and DELR1, respectively; and a kit comprising a container and first and second PCR primers that bind to DNA 3' or 5', respectively, of a splice site in the genomic DNA for a DPD gene for an exon encoding amino acids 581-635, and optionally wherein the first and second PCR primers hybridize under stringent conditions to nucleic acids complementary to DELF1 and DELR1, respectively. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 1 (claim 5 dependent thereon), 2 (claim 4 dependent thereon), 3, 6, 7 (claim 9 dependent thereon), 8, 10-14, 15 (claims 16 and 17 dependent thereon), 18, and 19 are so broad as to encompass a method of detecting a splicing defect in any DPD gene, comprising determining whether any genomic DNA encoding the DPD gene has any wild-type intron-exon boundary for any exon which encodes amino acids 581-635 for any corresponding wild-type DPD or a method of screening patients for sensitivity to 5-fluorouracil, comprising isolating any genomic DNA from the patient which encodes the DPD gene and determining whether the gene has any wild-type intron-exon boundary for any exon which encodes amino acids 581-635 for any corresponding wild-type DPD, and optionally, wherein the method comprises the step of amplifying any intronic genomic DNA encoding the DPD in the region flanking the exon that encodes amino acids 581-

635, and optionally, wherein the method comprises amplifying the genomic DNA with any primer that hybridizes to any DPD intronic nucleic acid that hybridizes to a primer selected from the group of primers consisting of DELF1 and DELR1; a composition comprising any first and second PCR primers that bind to DNA 3' or 5', respectively, of any splice site in any genomic DNA for a DPD gene for an exon encoding amino acids 581-635, and optionally wherein the first and second PCR primers bind to any intronic DPD DNA, and optionally wherein the first and second PCR primers hybridize under stringent conditions to any nucleic acids complementary to DELF1 and DELR1, respectively; and a kit comprising a container and any first and second PCR primers that bind to DNA 3' or 5', respectively, of any splice site in any genomic DNA for a DPD gene for an exon encoding amino acids 581-635, and optionally wherein the first and second PCR primers hybridize under stringent conditions to any nucleic acids complementary to DELF1 and DELR1, respectively. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of enzymes broadly encompassed by the claims. In this case the disclosure is limited to a method of detecting a splicing defect in a human DPD gene, comprising amplifying genomic DNA of a human DPD gene with primers DELF1 and DELR1 and determining whether a G to A transition occurs at nucleotide 1987 of genomic DNA encoding human DPD; a method of screening patients for sensitivity to 5-fluorouracil, comprising isolating human genomic DPD DNA from a patient and amplifying genomic DNA of a human DPD gene with primers DELF1 and DELR1 and determining whether a G to A transition occurs at nucleotide 1987 of genomic DNA encoding human DPD; a composition comprising a first PCR primer with the sequence

5'-TGCAAATATGTGAGGAGGGACC-3' and a second PCR primer with the sequence 5'-CAAAGCAACTGGCAGATTC-3'; and a kit comprising a container, a first PCR primer with the sequence 5'-TGCAAATATGTGAGGAGGGACC-3', and a second PCR primer with the sequence 5'-CAAAGCAACTGGCAGATTC-3'.

The specification does not support the broad scope of the claims which encompass any genomic DPD DNA, any wild-type intron-exon boundary, any intronic genomic DNA, and any PCR primer that binds to genomic DPD DNA because the specification does not establish: (A) a rational and predictable scheme for designing any primer that will amplify or hybridize to genomic DPD DNA from any source as not all genomic DPD DNA sequences from other organisms have been characterized; (B) a rational and predictable scheme for detecting splicing defects or sensitivity to 5-fluorouracil using genomic DPD DNA from any source, as not all DPD genes are completely homologous and therefore, the method provided in the specification would not be applicable to any genomic DPD DNA; (C) a rational and predictable scheme for detecting splicing defects or sensitivity to 5-fluorouracil using any primer that will hybridize to any genomic DPD gene or any intronic DPD DNA; (D) a rational and predictable scheme for detecting a splicing defect or sensitivity to 5-fluorouracil by screening for any mutant intron-exon boundary, as not all mutations in an intron-exon boundary of the human DPD gene will necessarily lead to a splicing defect and/or sensitivity to 5-fluorouracil and (E) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated

with the scope of the claims broadly including a method of detecting a splicing defect in any DPD gene, comprising determining whether any genomic DNA encoding the DPD gene has any wild-type intron-exon boundary for any exon which encodes amino acids 581-635 for any corresponding wild-type DPD or a method of screening patients for sensitivity to 5-fluorouracil, comprising isolating any genomic DNA from the patient which encodes the DPD gene and determining whether the gene has any wild-type intron-exon boundary for any exon which encodes amino acids 581-635 for any corresponding wild-type DPD, and optionally, wherein the method comprises the step of amplifying any intronic genomic DNA encoding the DPD in the region flanking the exon that encodes amino acids 581-635, and optionally, wherein the method comprises amplifying the genomic DNA with any primer that hybridizes to any DPD intronic nucleic acid that hybridizes to a primer selected from the group of primers consisting of DELF1 and DELR1; a composition comprising any first and second PCR primers that bind to DNA 3' or 5', respectively, of any splice site in any genomic DNA for a DPD gene for an exon encoding amino acids 581-635, and optionally wherein the first and second PCR primers bind to any intronic DPD DNA, and optionally wherein the first and second PCR primers hybridize under stringent conditions to any nucleic acids complementary to DELF1 and DELR1, respectively; and a kit comprising a container and any first and second PCR primers that bind to DNA 3' or 5', respectively, of any splice site in any genomic DNA for a DPD gene for an exon encoding amino acids 581-635, and optionally wherein the first and second PCR primers hybridize under stringent conditions to any nucleic acids complementary to DELF1 and DELR1, respectively. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24

(CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. Claims 1-3, 6-8, 10-12, 15, and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gonzalez et al. (Trends Pharmacol Sci 16:325-327; provided with application) in view of Meinsma et al. (DNA Cell Biol 14:1-6; 1995; provided with application). Claims 1-3 and 6-8 are drawn to methods for detecting a splicing defect in a dihydropyrimidine dehydrogenase (DPD) gene or methods of screening patients for sensitivity to 5-fluorouracil by detecting a splicing defect in a DPD gene by determining the presence of a wild-type intron-exon boundary for an exon encoding amino acids 581-635 of DPD.

Gonzalez et al. teach that DPD deficiency has been shown to be associated with acute 5-FU toxicity (p 325, columns 1 and 2) and that patients exhibiting DPD deficiency have a 165-bp deletion in DPD mRNA (p 327, left column). Gonzalez et al. further teach that the intron-exon boundaries of the DPD gene are being determined in order to develop a convenient screening assay for the analysis of cancer patients having DPD gene

mutations, and that by determining the intron-exon boundaries of the DPD gene, specific PCR primers could be designed to analyze for mutant DPD genes using a PCR-based screening procedure. Gonzalez et al. do not teach methods for detecting a splicing defect in a DPD gene or methods of screening patients for sensitivity to 5-fluorouracil by detecting a splicing defect in a DPD gene

Meinsma et al. teach that patients exhibiting DPD deficiency have a 165-bp deletion in DPD mRNA (p 3, Results, paragraph 3) and that this 165-bp deletion corresponds to a deletion of amino acids 581-635 of the DPD polypeptide (p 3, Results, paragraph 3). Meinsma et al. teach that the 165-bp deleted exon is the result of a mutation that causes defective splicing of the DPD gene (p 3, Results, paragraph 3).

Therefore, it would have been obvious to one of ordinary skill in the art to combine the teachings of Gonzalez et al. and Meinsma et al. for methods for detecting a splicing defect in a DPD gene or methods of screening patients for sensitivity to 5-fluorouracil by detecting a splicing defect in a DPD gene by determining the presence of a wild-type intron-exon boundary for an exon encoding amino acids 581-635 of DPD or a composition or a kit comprising a first PCR primer which binds 3' of a splice site in the genomic DNA for a DPD gene for an exon encoding amino acids 581-635, and a second PCR primer which binds 5' of a splice site in the genomic DNA for a DPD gene for an exon encoding amino acids 581-635, and optionally, wherein the first PCR primer binds to intronic DPD DNA, and optionally, wherein the second PCR primer binds to intronic DPD DNA, and optionally, wherein the kit comprises instructions. One would have been motivated for methods for detecting a splicing defect in a DPD gene or methods of screening patients for sensitivity to 5-fluorouracil by detecting a splicing defect in a DPD

gene or a composition or a kit comprising PCR primers because of the teachings of Gonzalez et al. as described above. One would have a reasonable expectation of success for methods for detecting a splicing defect in a DPD gene or methods of screening patients for sensitivity to 5-fluorouracil by detecting a splicing defect in a DPD gene or a composition or a kit comprising PCR primers because of the results of Gonzalez et al. and Meinsma et al. Therefore, claims 1-3, 6-8, 10-12, 15, and 16, drawn to a methods for detecting a splicing defect in a DPD gene or methods of screening patients for sensitivity to 5-fluorouracil by detecting a splicing defect in a DPD gene or a composition or a kit comprising PCR primers would have been obvious to one of ordinary skill in the art.

16. Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Meinsma et al. in view of Gonzalez et al. as applied to claims 1-3, 6-8, 10-12, 15, and 16 above and further in view of Roy et al. (Singapore J Obstet Gyn 26:176-186; provided with application). Claim 5 is drawn to a method of detecting a splicing defect in a DPD gene, wherein the sequence of the intron-exon boundary is determined using an oligonucleotide array.

Meinsma et al. and Gonzalez et al. disclose the teachings as described above.

Roy et al. generally teach a review of methods of detecting genetic mutations for diagnosing inherited disease. Specifically, Roy et al. teach a method of detecting single base polymorphisms by hybridization of PCR-amplified genomic DNA to an allele-specific oligonucleotide (p 178, left column, bottom). Roy et al. further teach "an innovative adaption of this technique is reverse allele-specific hybridization, in which unlabelled synthetic oligonucleotide probes complementary to normal or specific mutant

sequences are bound to solid supports and hybridized with labeled DNA amplified by PCR from genomic DNA" (p 178, right column, middle).

Although Roy et al. do not specifically teach a method of detection using an oligonucleotide array, it would have been obvious to one of ordinary skill in the art at the time of the invention that oligonucleotide probes bound to a solid support as described by Roy et al. was an oligonucleotide array. Therefore, it would have been obvious to one of ordinary skill in the art to combine the teachings of Meinsma et al., Gonzalez et al., and Roy et al. for a method of detecting a splicing defect in a DPD gene, wherein the sequence of the intron-exon boundary is determined using an oligonucleotide array. One would have been motivated for a method of detecting a splicing defect in a DPD gene, wherein the sequence of the intron-exon boundary is determined using an oligonucleotide array because of the teachings of Roy et al. as described above and the reduction in assay processing time that would have been obvious to one of ordinary skill at the time of the invention. One would have a reasonable expectation of success for a method of detecting a splicing defect in a DPD gene, wherein the sequence of the intron-exon boundary is determined using an oligonucleotide array because of the teachings of Meinsma et al., Gonzalez et al., and Roy et al.. Therefore, claim 5, drawn to a method of detecting a splicing defect in a DPD gene, wherein the sequence of the intron-exon boundary is determined using an oligonucleotide array would have been obvious to one of ordinary skill in the art.

17. No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (703) 308-3934. The examiner can normally be reached Monday-Friday from 8:00 am to 4:30 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX number for this Art Unit is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.
David J. Steadman

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PRIMARY EXAMINER
GROUP ~~1800~~
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